In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 18-1418V

Filed: August 29, 2022

TRICIA SWITZER, As Executor of the Estate of Richard Feider, Sr., Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	TO BE PUBLISHED Decision on Entitlement; Influenza Vaccine; Pneumococcal Vaccine; Systemic Inflammatory Response Syndrome ("SIRS"); Multiple Organ Dysfunction Syndrome ("MODS"); Acute Kidney Injury ("AKI").

Andrew Downing, Downing, Allison & Jorgenson, Phoenix, AZ, for Petitioner
Voris Johnson, U.S. Department of Justice, Washington, DC, for Respondent

DECISION ON ENTITLEMENT[1]

Oler, Special Master:

On September 17, 2018, Tricia Switzer ("Petitioner"), as executor of the estate of Richard Feider, Sr. (hereinafter "Mr. Feider" or "Vaccinee"), filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10, *et seq*.[2] (the "Vaccine Act" or "Program") alleging that Mr. Feider suffered from vaccine-induced Systemic Inflammatory Response Syndrome ("SIRS") that progressed to multiple organ dysfunction and death, and which resulted from the influenza and Prevnar 13 vaccinations he received on

[1] This Decision will be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided in 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the Decision's inclusion of certain kinds of confidential information. To do so, each party may, within 14 days, request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, this Decision will be available to the public in its present form. *Id.*

[2] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

September 20, 2016. Pet. at 1, 7. For the reasons discussed in this decision, I find that although Petitioner presented preponderant evidence that the flu vaccine can cause SIRS, she has not demonstrated that that the vaccines Mr. Feider received "did cause" his condition.

I. Procedural History

Petitioner filed a petition on September 17, 2018, alleging that Mr. Feider developed vaccine-induced SIRS from the influenza and Prevnar 13 vaccinations he received on September 20, 2016. Pet. at 1, 7. Petitioner claimed these vaccinations resulted in Mr. Feider's subsequent death on October 9, 2016. *Id.* at 6, 8.

Petitioner filed medical records on September 20, and September 25, 2018. Exs. 1-6, 7-8. On July 11, 2019, Respondent filed a Rule 4(c) Report stating Petitioner has not met her burden of proving entitlement to compensation under the Vaccine Act. Resp't's Rep. at 14.

Between October 2019 and July 2020, the parties filed a series of expert reports from their respective experts, Dr. Shoenfeld, Dr. Fife, and Dr. Morel. Exs. 9, A, C, 40, 41, AA, and BB.

I held a status conference on August 20, 2020 and then issued an order with additional questions for both parties' experts. *See* Scheduling Order dated August 21, 2020, ECF No. 35.

On September 1, 2020, Petitioner filed an expert report from Dr. Shoenfeld responding to my questions. Ex. 56. On October 19, 2020, Respondent filed reports from Drs. Fife and Morel. Exs. HH, JJ.

On February 19, 2021, Petitioner filed a Motion for a Ruling on the Record. ECF No. 40. On April 20, 2021, Respondent filed a response. ECF No. 41. On May 18, 2021, Petitioner filed a reply brief. ECF No. 42. On June 14, 2021, the parties filed a joint status report indicating the record was complete, and that this matter was now ripe for a decision. ECF No. 44.

II. Medical Records

A. Relevant Pre-Vaccination History

Mr. Feider had a prior medical history that included coronary artery disease requiring a four-vessel bypass, aortic stenosis requiring an aortic valve replacement in 2013 (Ex. 3 at 1), peripherical vascular disease (Ex. 4 at 1), hypertension, hyperlipidemia, renal vascular disease, a heart murmur. He was previously a cigarette smoker. *See* Ex. 8 at 281 (noting he smoked 40 pack years, and quit in 1984).

On July 19, 2016, Mr. Feider visited Dr. Inkee Min, a nephrologist, at the Buffalo Medical Group for a follow-up appointment related to his chronic renal failure due to hypertensive nephrosclerosis and atrophic right kidney. Ex. 4 at 54-55. In a letter written by physician assistant ("PA") Robert Hynes, it was noted that Mr. Feider's renal function was stable. *Id.*

On September 20, 2016, Mr. Feider received the influenza vaccination in his right deltoid and the pneumococcal (Prevnar 13) vaccination in his left deltoid. Ex. 2 at 1; Ex. 8 at 996. He was 72 years old at the time of vaccination.

B. Post-Vaccination History

Mr. Feider was transported to the Buffalo Veterans Affair ("VA") Hospital ER department via ambulance on September 24, 2016. Mr. Feider reported that he had received the influenza and pneumococcal vaccines on September 20th and the following day, developed a cough, felt feverish and unwell. Ex. 8 at 982. Mr. Feider stated he felt better on Thursday and most of the day on Friday (September 23rd), but late that night experienced a sudden onset of shortness of breath and difficulty breathing. *Id.* Mr. Feider had a fever of 104.5ºF and was started on solumedrol. *Id.* at 980. Mr. Feider underwent an EKG, x-ray, and blood samples were taken for cultures. *Id.* The leading diagnosis was pneumonia and sepsis. *Id.* at 985. Mr. Feider had rales in both lungs, left more than right, and was experiencing mildly labored breathing. *Id.* at 984.

On the same day, Mr. Feider was examined by Dr. Jaime Bittner who recorded the following history of present illness:

> Patient presents with a one day history of sudden SOB (shortness of breath) with fever. Patient felt relatively healthy yesterday and went to his usual cardio rehab, went home had lunch, went out to dinner and felt like his usual self. He was watching TV last night and at 11pm began to feel warm, shaky, and had a "tough time breathing"…. Patient got a Flu shot and pneumovax on Tuesday, then felt warm and slept all day Wednesday but was back to his usual state of health by Thursday.

Ex. 8 at 946. Mr. Feider's fever was 100.2ºF. *Id.* at 947. The EKG, x-ray, and cultures were negative for the most common infectious sources. *Id.* at 102, 241-43. Mr. Feider's active issues included shortness of breath, fever, leukocytosis, AKI (acute kidney injury), CKD (chronic kidney disease), hypokalemia, history of CAD (chronic artery disease), and HTN (hypertension). *Id.* at 952-53.

On the same day, Mr. Feider was also seen by Dr. Vasvi Singh, a cardiology fellow, and Dr. Sunil Baldwa, a cardiologist, for a cardiology consult. Ex. 4 at 343-45, 349-51. Drs. Singh and Baldwa diagnosed Mr. Feider with severe sepsis, mild troponin elevation, status post bioprosthetic aortic valve replacement and coronary artery bypass grafting, sinus bradycardia, severe peripheral arterial disease, hypertension, and hyperlipidemia. *Id.* at 350. Mr. Feider's sepsis was treated with antibiotics and hydration. *Id.* Around 10:45pm on September 24, 2016, Mr. Feider's temperature was down to 97.4ºF. *Id.* at 56.

During the early morning hours of September 25, 2016, Mr. Feider began experiencing hypoxic respiratory failure, prompting a transfer to the ICU and intubation with mechanical ventilation. Ex. 8 at 899-901. Mr. Feider had diffuse crackles in all lung fields bilaterally. *Id.* at 900. Mr. Feider was subsequently seen by Drs. Adil Shujaat and Benjamin Segerson, internal medicine doctors, that same day. *Id.* at 887-92. Mr. Feider was given an arterial line placement in

his right wrist and hemodialysis catheter. *Id.* at 904. Dr. Rajiv Ranjan, a nephrologist, noted that Mr. Feider was not producing urine and his renal function was continuing to deteriorate. *Id*. at 872.

On September 26, 2016, Mr. Feider was seen by Dr. Thomas Russo, an infectious diseases consultant, for "hypoxic respiratory failure, possible pneumonia." Ex. 8 at 323-25. Dr. Russo noted that Mr. Feider's sputum culture contained "very rare red blood cells, 1-2+ white blood cells, very rare squamous epithelial cells,…" *Id.* at 324-25. Mr. Feider's x-ray revealed mild interval improvement of pulmonary edema, and superimposed infection could not be completely excluded. *Id.* at 325. It was Dr. Russo's impression that Mr. Feider was experiencing acute hypoxic respiratory failure and had possible community acquired pneumonia. *Id.* at 325. Dr. Russo also noted it was "difficult to differentiate pulmonary edema from extensive bilateral pneumonia." *Id.*

On the same day, Mr. Feider was seen for a cardiology consultation. Ex. 4 at 446-53. It was noted that his condition was either pneumonia, idiopathic pneumonia, acute respiratory distress syndrome (ARDS), or pulmonary edema. *Id.* at 448. Mr. Feider's CT scan was negative for a stroke. *Id.* Mr. Feider's echocardiogram revealed mild concentric left ventricular hypertrophy, mild to moderate mitral regurgitation, and mild to moderate valvular aortic stenosis. *Id*. at 447.

On September 27, 2016, Dr. Jahan Porhomayon, a critical care doctor, observed Mr. Feider's symptoms related to his congestive heart failure and hypertension had improved with dialysis. Ex. 8 at 812. Mr. Feider's hypoxia has also improved but had developed a rash or petechia with unknown etiology. *Id.*

On September 28, 2016, Mr. Feider was seen for a hematology consult for his anemia and a worsening thrombocytopenia. *Id.* at 315, 320. Mr. Feider had a history of thrombocytopenia with a baseline range of 95,000-120,000 platelets since 2011. *Id.* at 315. Mr. Feider was anemic upon admission. *Id.* Mr. Feider's platelet count had dropped to 60,000 at one point but had rebounded to 83,000. *Id.* at 320.

On September 30, 2016, Mr. Feider underwent a failed extubation. Ex. 8 at 739-40, 42. Dr. Russo returned to Mr. Feider the same day and assessed him as follows: "?? CAP [community-acquired pneumonia]- finishing 7 days of antibiotics today. I suspect his pulmonary failure is probably not due to infection." *Id.* at 732.

On October 1, 2016, Mr. Feider was noted to be afebrile after antibiotics and his white blood cell count was at 8.7 (normal). Ex. 8 at 702. Dr. Pietrantoni, a pulmonary and critical care physician, noted that it was unlikely to be CAP (community acquired pneumonia) given these improvements and the pneumonia had resolved. *Id.* at 702, 705. Mr. Feider was given additional dialysis, which he seemed to have tolerated well. Mr. Feider was also anuric. *Id.* at 703.

On October 2, 2016, Mr. Feider underwent a head and lung CT. Ex. 8 at 624. Dr. Amy Kao interpreted Mr. Feider's chest CT and noted that his "heart shadow is accentuated by AP technique and appears mildly enlarged. Trachea is deviated to the right as before… diffuse interstitial pattern persists. Findings are nonspecific but may relate to ARDS or pulmonary edema." *Id.* at 625. Dr.

Alice Smith interpreted the head CT and noted "age-related changes without evidence of acute intracranial event." *Id.*

On October 3, 2016, a bronchoscopy was performed on Mr. Feider. Ex. 8 at 634-36. The findings revealed:

> normal carina, no endobronchial masses/lesions seen. Right upper lobe bronchial tree appeared normal. There was bloody secretion coming out the RML (right middle lobe) and RLL (right lower lobe). Also RLL and RML mucosa appeared erythematous. Left upper lobe bronchial tree was normal. There were also bloody secretions coming the LLL (left lower lobe) and the mucosa was erythematous. No endobronchial lesions or masses.

Id. at 635-36. Samples were also taken during the bronchoscopy from the RLL and LLL which revealed: acute inflammation, blood and mucoid material,… no evidence of fungal, bacterial or acid fast micro-organisms on GMS, Gram and AFB special stain in the RLL; and rare atypical degenerate squamous epithelial cells were seen in the LLL. *Id.* at 1001. The samples were grown for five days and showed no growth of microorganisms. *Id.* at 235-37.

On October 5, 2016, Dr. John Sellick Jr., another infectious diseases consultant, visited Mr. Feider again because his WBC had risen to 30,000. Ex. 8 at 280-83. Mr. Feider also had a temperature of 100.6ºF. *Id.* at 281. Dr. Sellick noted that Mr. Feider's cultures were negative, with the exception of yeast, which was unlikely to be pathogenic. *Id.* at 282. Mr. Feider resumed antibiotics. *Id.* at 283.

In the early hours of October 6, 2016, Mr. Feider was observed to hypotensive and was not responding to IV fluids. Ex. 8 at 467, 475. Mr. Feider's WBC was decreasing but his ALT (alanine transaminase) and AST (aspartate aminotransferase) levels were rising. *Id.* at 472-73. In a nephrology note, it was noted that "[Mr. Feider] was getting [hemodialysis] but [blood pressure] started to decrease and currently has been started on levophed[3] due to hypotension." *Id.* at 460. Mr. Feider was removed from levophed the next day. *Id.* at 253.

On October 8, 2016, Mr. Feider underwent another head and chest CT and was noted to have hypodensities concerning for a stroke. Ex. 8 at 412. The chest CT revealed "diffuse fluffy opacities which could representing [sic] pulmonary edema, ARDS or pneumonia. Without significant change from last exam." *Id.* at 403. The ICU resident informed Mr. Feider's family that the stroke possibly affected the occipital lobe, parietal lobe, and possibly the brainstem, and Mr. Feider's prognosis was "not very good." *Id.* at 396.

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[3] Levophed: trademark for a preparation of norephinephrine bitartrate, Dorland's Online Medical Dictionary, *Levophed*, https://www.dorlandsonline.com/dorland/definition?id=28164. Norepinephrine bitartrate is "used to restore the blood pressure in certain cases of acute hypotension, and to improve cardiac function during decompensation associated with congestive heart failure or cardiovascular surgery, administered intravenously." *Norepinephrine bitartrate*, https://www.dorlandsonline.com/dorland/definition?id=93415 (last accessed August 16, 2022).

On October 9, 2016, Mr. Feider underwent a chest x-ray which revealed: "similar central pulmonary vascular congestion and diffuse interstitial opacities, most confluent at the lung bases, which could be due to pulmonary edema versus pneumonia." Ex. 8 at 376. The ICU doctors informed Mr. Feider's family that he was unresponsive and suffered a stroke. *Id.* at 396-97. Mrs. Feider asked for life support be discontinued and Mr. Feider died on October 9, 2016 at 5:14p.m. *Id.* at 371-74.

Dr. Porhomayon, an ICU attending physician, authored Mr. Feider's discharge summary. Ex. 8 at 248-49. Mr. Feider's primary diagnosis was "death [secondary to] multiple organ dysfunction syndrome." *Id.* at 248. Secondary diagnoses treated included:

> septic shock, acute renal failure, hyperkalemia, hyperphosphatemia, hypermagnesemia, acute hypoxic respiratory failure, acute cerebrovascular accident, community-acquired pneumonia, flash pulmonary edema, hypertensive emergency, hypertension, hypotension requiring vasopressors, anemia, renal artery stenosis, coronary artery disease with bypass grafting, chronic kidney disease, hyperlipidemia, peripheral vascular disease s/p aortofemoral bypass graft, carotid stenosis, aortic valve replacement, peripheral neuropathy, hypokalemia, hypocalcemia, hypomagnesemia, malnutrition, transaminitis, rhabdomyolysis, muscle wasting, constipation, thrombocytopenia, delirium/agitation, ? propofol infusion syndrome, and ? ARDS.

Id. at 248-49.

III. Petitioner's Statement

Ms. Switzer filed a statement with her petition, recounting the events in late September to October 2016. Ex. 1. Ms. Switzer provided some background information on her father, Richard Feider, Sr. *Id.* at 1. Mr. Feider retired from the U.S. Postal Service in 2002 and was happily married for 49 years. *Id.* at 1. Mr. Feider was a veteran of the Air Force and had been on active duty in Vietnam. *Id.*

Mr. Feider attended a medical appointment on September 20, 2016, when he also received the flu and pneumonia vaccines. Ex. 1 at 2. Subsequently, he returned home, ate lunch and within a few hours began to feel unwell. *Id.* He stated he had a headache, was feeling tired and achy, and went to bed early. *Id.* The next day, Mr. Feider remained in bed with a fever and had flu-like symptoms. *Id.*

On September 23, 2016, Mr. Feider had difficulty breathing and body shakes; he was taken to the "Veteran's Hospital ER." Ex. 1 at 2. He was given oxygen for his breathing issues and tested for flu and pneumonia based on his symptoms. *Id.* Mr. Feider was soon admitted and prophylactic antibiotics and medication were given to reduce Mr. Feider's fever. *Id.* Ms. Switzer stated hospital staff believed that Mr. Feider could have contracted the flu or pneumonia when he got his shots, or alternatively they stated his illness was "too coincidental and was likely related to the shot." *Id.* Mr. Feider remained in good spirits although he was not improving. On September 25, 2016, Ms.

Switzer returned to the hospital and saw Mr. Feider intubated and in a drug-induced coma. *Id.* at 3. Doctors were also concerned about Mr. Feider's kidneys at this time. *Id.*

Mr. Feider's condition worsened over the next two weeks. Ex. 1 at 3. Ms. Switzer recalls a nurse telling her mother that she believed he was having a severe reaction to his vaccination. *Id.* A doctor informed them that Mr. Feider's cultures were negative for flu and pneumonia so it couldn't have been the shot. *Id.* Mr. Feider began to fill up with fluid because of his low-functioning kidneys; the hospital was performing dialysis every other day. *Id.*

On October 6, 2016, Mr. Feider was undergoing dialysis when his blood pressure dropped. Ex. 1 at 3. On October 8, 2016, Mr. Feider underwent a "brain scan" and the doctors stated that he may have had a stroke during the October 6, 2016 dialysis session as he had very low brain activity. *Id.*

On October 9, 2016, Petitioner gathered with the rest of her family at the hospital where they were informed that Mr. Feider was septic, his organs were failing, and there was no chance of recovery. *Id.* Mr. Feider was removed from life support that day. *Id.*

Ms. Switzer states that the medical professionals were not able to give her a diagnosis, but his death certificate listed his cause of death as multisystemic organ failure due to sepsis pneumonia. Ex. 1 at 4. This statement was signed by Ms. Switzer on September 14, 2018. *Id.*

IV. Expert Opinions and Qualifications

A. Petitioner's Expert: Dr. Yehuda Shoenfeld

1. Qualifications

Dr. Shoenfeld founded The Center for Autoimmune Disease at Sheba Medical Center, which is affiliated with the Sackler Faulty of Medicine at Tel-Aviv University. Ex. 9 at 1. He was the Laura Schwarz-Kipp Chair for Research of Autoimmune Diseases at Tel-Aviv University and an Emeritus professor at Tel-Aviv University, teaching medical students and research candidates. *Id*. Dr. Shoenfeld's research focuses on autoimmune and rheumatic diseases, and he has published more than 2060 peer-reviewed papers. *Id*. Dr. Shoenfeld has also authored and edited 28 books and is on the editorial boards of 32 journals in the field of autoimmunity and rheumatology. *Id.* at 1-2.

2. Expert Reports

Dr. Shoenfeld filed four expert reports in this case. Exs. 9 (hereinafter "First Shoenfeld Rep."), 40 (hereinafter "Shoenfeld Response to Fife"), 41 (hereinafter "Shoenfeld Response to Morel"), and 56 (hereinafter "Shoenfeld Response to Questions").

In his first expert report, Dr. Shoenfeld theorized that concomitant administration of the quadrivalent inactivated influenza vaccine and the 13-valent pneumococcal conjugate vaccine caused Mr. Feider to develop SIRS, respiratory failure with signs of interstitial lung disease (ILL),

and acute kidney injury and ultimately, death. First Shoenfeld Rep. at 9. Dr. Shoenfeld opined that receiving vaccinations, along with undergoing major surgery, suffering an infection, or experiencing major trauma, may trigger a systemic inflammatory response in the body. *Id.* Maintaining a proper balance of pro- and anti-inflammatory cytokines is critical to regulating the body's systemic inflammatory response; any dysregulation of this balance can lead to SIRS and Multi-Organ Dysfunction Syndrome (MODS). *Id.* at 10. Dr. Shoenfeld stated that Mr. Feider's symptoms were consistent with the diagnostic criteria for SIRS, including tachycardia, tachypnea, leukocytosis,[4] fever or hypothermia, and leukopenia,[5] or bandemia.[6] *Id.* at 11. Dr. Shoenfeld also suggested that the lack of a confirmed infection made SIRS the proper diagnosis of Mr. Feider's condition. *Id*.

Dr. Shoenfeld drew parallels between Mr. Feider's clinical progression with cases of SIRS in six volunteers that were triggered by an intravenous dose of a superagonist anti-CD28 monoclonal antibody (mAb),[7] a T cell surface activation marker, that led to rapid induction of pro-inflammatory cytokines. First Shoenfeld Rep. at 11. All six patients developed initial clinical signs consistent with the criteria for SIRS, and they later displayed respiratory distress, pulmonary infiltrates, and renal impairment, mirroring Mr. Feider's course. *Id*. *citing* Suntharalingam et al., *Cytokine Storm in Phase 1 Trial of the Anti-CD28 Monoclonal Antibody TGN1412,* 355 N ENG J MED 10, 1018-28 (2006) (filed as Ex. 39).

Dr. Shoenfeld pointed out that acute lung injury (ALI) and acute kidney injury (AKI) were both present in Mr. Feider, and that ALI and its more severe form – acute respiratory distress syndrome (ARDS) – can lead to respiratory failure. First Shoenfeld Rep. at 12. Dr. Shoenfeld

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[4] Leukocytosis is "a transient increase in the number of leukocytes in the blood; seen normally with strenuous exercise and pathologically accompanying hemorrhage, fever, infection, or inflammation." *Leukocytosis*, Dorland's Online Med. Dictionary, https://www.dorlandsonline.com/dorland/definition?id=28055&searchterm=leukocytosis (last accessed August 18, 2022).

[5] Leukopenia is "reduction in the number of leukocytes in the blood below about 5000 per mm." *Leukopenia*, Dorland's Online Med. Dictionary, https://www.dorlandsonline.com/dorland/definition?id=28093&searchterm=leukopenia (last accessed August 18, 2022).

[6] Bandemia is a finding that involves "[t]he presence of more than 6% of immature neutrophils (band cells) in the blood. This finding indicates infection, inflammation, or some other significant physical stress." *Bandemia*, TABER'S CYCLOPEDIC MEDICAL DICTIONARY 243 (23d ed. 2017).

[7] "Monoclonal antibodies are synthesized by a single clone of B lymphocytes or plasma cells and have identical structure and antigen specificity…. The identical copies of the antibody molecules produced contain only one class of heavy chain and one type of light chain… monoclonal antibodies (mAbs) are produced in large quantities against a plethora of antigens for use in diagnosis and sometimes treatment. mAbs are homogenous and widely employed in immunoassays, single antigen identification mixtures, delineation of cell surface molecules, and assays of hormone and drugs in serum, among other uses… Monoclonal antibodies have been radioactively labeled and used to detect tumor metastases, to differentiate subtypes of tumors with monoclonal antibodies against membrane antigens or intermediate filaments, to identify microbes in body fluids, and for circulating hormone arrays. mAbs may be used to direct immunizations or radioisotopes to tumor targets with potential for tumor therapy." *Illustrated Dictionary of Immunology* 504-05 (3d ed. 2009).

suggested that Mr. Feider's older age contributed to a different immune response signature to the influenza vaccine than normal. A normal post-vaccination type 1 cytokine signature would be characterized by IFN-γ cytokine, but a study showed that only TNF-α was associated with seroconversion after influenza vaccination in elderly subjects. *Id.* at 13; *citing* Bloch et al., *Production of TNF-alpha ex vivo is predictive of an immune response to flu vaccination in a frail elderly population*, 27 EUR CYTOKINE NETW 3, 63-67 (2016) (filed as Ex. 24). Dr. Shoenfeld opined that Mr. Feider's SIRS was caused by an elevation of pro-inflammatory cytokines such as TNF-α to compensate for his defective influenza-specific IFN-γ response, related partially to age. First Shoenfeld Rep. at 13. While Dr. Shoenfeld admitted that systemic inflammatory reactions to influenza vaccines are very rare, certain genetic predispositions may be involved with polymorphisms of receptor antagonists that could lead to the uncontrolled inflammation that is a central component of ALI/ARDS. *Id.* Dr. Shoenfeld theorized that, although the definitive cause of Mr. Feider's AKI was not identified, severe body pain and highly elevated creatine kinase levels matched the diagnostic criteria for rhabdomyolysis;[8] he cited nine cases of AKI induced by rhabdomyolysis following influenza vaccination to support his claim. *Id.* at 14.

Dr. Shoenfeld challenged Dr. Fife's proposition that Mr. Feider developed community-acquired pneumonia, pointing to the interpretation of the X-ray images and chest CT as having "differential considerations includ[ing] pulmonary edema, ARDS or diffuse pneumonia." Shoenfeld Response to Fife at 2. Dr. Shoenfeld stated that the diagnosis of community acquired pneumonia was not substantiated and was questioned by the infectious diseases consultant, who noted, "Pneumonia – difficult to say if he has a pulmonary infection. However, he did present with a fever of 104+ and has no other clear source." *Id.* at 2-3; citing Ex. 8 at 326. According to the Infectious Diseases Society of America guidelines, "a failure of treatment or a deterioration in hospitalized patients with community-acquired pneumonia should have been considered after 72 hours of initial treatment" and should lead to a complete re-evaluation of the patient to potentially uncover an alternative diagnosis. *Id.* at 2. Instead, treatment with antibiotics continued and was not effective. *Id*. Dr. Shoenfeld pointed out that ARDS was included in the differential diagnosis, and ARDS belongs to the group of ILL. *Id.* at 3. Dr. Shoenfeld charged that the prior published case reports showing SIRS and lung injury induced by the same vaccines made his assessment more credible than the lack of comprehensive patient evidence did for a diagnosis of community acquired pneumonia. *Id*.

Dr. Shoenfeld also filed an expert report in response to Dr. Morel's report. Dr. Shoenfeld challenged Dr. Morel's assertion that "there is no literature to suggest that any vaccine can lead to the set of symptoms that would justify the diagnosis of SIRS". Shoenfeld Response to Morel at 2. Immune response in adults is normally less intense than in children because of developed immunity and previous exposure to the same vaccines. *Id*. However, Dr. Shoenfeld noted that there are at least 10 published cases of adults developing SIRS after receiving influenza or pneumococcal vaccines, five of which involved patients aged 57-86. *Id*. Dr. Shoenfeld addressed Dr. Morel's claims about the administration of mAb targeting CD28. Dr. Morel argued that the immune response following mAb administration would be stronger than a natural response to

[8] Rhabdomyolysis is the "disintegration or dissolution of muscle, associated with excretion of myoglobin in the urine." *Rhabdomyolysis*, Dorland's Online Med. Dictionary, https://www.dorlandsonline.com/dorland/definition?id=43665&searchterm=rhabdomyolysis (last accessed August 18, 2022).

vaccination, though she admitted that Mr. Feider's age and atherosclerosis were both factors that were associated with an increased inflammatory environment. *Id*. Dr. Shoenfeld opined regarding the causal chain between those factors and Mr. Feider's illness. Dr. Shoenfeld argued that vaccination could still lead to the same overall inflammatory context that was observed in Mr. Feider, particularly if there was a genetic predisposition to exaggerated inflammatory-immune response to pneumococcal vaccines. *Id.* at 3. Dr. Shoenfeld defended his claim by pointing out that the pneumonia diagnosis was questioned by the infectious diseases expert, that the sputum gram stain was negative at the time of testing in confirming pneumonia, and that antibiotics were ineffective in treating Mr. Feider's condition. *Id*.

Dr. Shoenfeld also addressed Dr. Morel's theory about T cell response and cytokine production being confined to the lymph nodes and evading wider detection in the systemic circulation. Shoenfeld Response to Morel at 3. Dr. Shoenfeld noted that none of the 26 patients in Dr. Morel's cited study developed SIRS after receiving the flu vaccine, making it difficult to draw conclusions about cytokine levels and distribution in patients who develop SIRS. *Id*. Dr. Shoenfeld suggested that the short half-life of cytokines in the blood also makes them difficult to detect, but that more stable biomarkers correlated with pro-inflammatory cytokines in SIRS like C-reactive protein (CRP) have been found at elevated levels in at least four cases of SIRS following influenza or pneumococcal vaccination. *Id*. Dr. Shoenfeld conceded that the fact that CK levels did not rise until 10 days into Mr. Feider's course suggested that rhabdomyolysis did not start until late in the case and could not have caused AKI. *Id.* at 4. Dr. Shoenfeld still argued that AKI could be caused by vaccination, highlighting that AKI is one of the most common dysfunctions in SIRS. *Id*.

B. Respondent's Expert: Dr. Kenneth Fife

1. Qualifications

Dr. Fife received his medical degree and Ph.D. in microbiology from Johns Hopkins University. Ex. B (hereinafter "Fife CV") at 1. Dr. Fife is an Emeritus Professor of Medicine in the Division of Infectious Diseases at the Indiana University School of Medicine. Fife CV at 1. He is a Fellow of the American College of Physicians and a fellow of the Infectious Diseases Society of America. *Id*. Dr. Fife has written 151 peer-reviewed publications, is board certified in internal medicine, and is board eligible in infectious diseases. *Id*.

2. Expert Reports

Dr. Fife filed three expert reports in this case. Exs. A (hereinafter "First Fife Rep."), AA (hereinafter "Second Fife Rep."), and HH (hereinafter "Third Fife Rep."). Dr. Fife theorized that Mr. Feider developed community-acquired pneumonia more than three days after receiving and independent of the influenza and pneumococcal conjugate vaccines. First Fife Rep. at 2-3. Dr. Fife noted that Mr. Feider's symptoms of fatigue and subjective fever (said he "felt warm") a day after receiving the vaccines were commonly experienced symptoms shortly after receiving either the influenza or the pneumococcal conjugate vaccines. *Id.* at 2. Mr. Feider received regular influenza vaccinations between 2008 and 2013 as well as the pneumococcal polysaccharide vaccine in 2013 but never showed any significant reactions to those immunizations. *Id.* at 1. He reported feeling normal the following days and was able to resume normal activities without disturbance, including

participating in cardiac rehab exercises and going out to dinner, and Dr. Fife noted that this was consistent with Mr. Feider's lack of history of significant reactions to those immunizations. *Id.* The recurrence of feelings of warmth as well as a non-productive cough and shortness of breath only developed around 11 pm on the third day after the administration of the vaccinations. *Id.* at 2. Although many medical providers noted that Mr. Feider received two vaccinations before arriving at the hospital, none attributed his symptoms or condition to the vaccines, and community-acquired pneumonia was listed on the discharge (death) summary. *Id*.

Dr. Fife discussed Dr. Shoenfeld's arguments, pointing out that SIRS is a vague set of signs/symptoms present in many infections and in inflammatory conditions, including pneumonia, and that temporal proximity of the symptoms with the vaccinations was not dispositive of any causal relationship between them. First Fife Rep. at 3. Dr. Fife also disagreed with Dr. Shoenfeld's conclusion that "[t]here are no other causes to explain this deterioration after the vaccine", saying that Dr. Shoenfeld completely ignored the diagnosis of community-acquired pneumonia given by every provider who evaluated Mr. Feider. *Id*.

Dr. Fife noted that an admission sputum smear was not diagnostic and all blood cultures were negative in confirming an infection; however he emphasized that sputum smears "are positive in only about one-third of cases of community-acquired pneumonia and nearly half of all cases of severe sepsis have negative blood cultures." First Fife Rep. at 3. Additionally, Mr. Feider's cough was non-productive and was unlikely to produce a useful sputum specimen. *Id.* Dr. Fife pointed out that although the bronchoalveolar lavage fluid lacked microorganisms like bacteria that would indicate pneumonia, that result was unsurprising because Mr. Feider had been taking antibiotics for 10 days before the procedure. *Id.* at 1. Dr. Fife noted that negative smear tests and cultures during treatment do not exclude a possible pneumonia diagnosis, and Mr. Feider's underlying conditions and presenting symptoms gave him "about a 1 in 3 chance of dying of pneumonia during this hospitalization, so the ultimate outcome is not surprising." *Id.* at 3.

Dr. Fife's second report was filed in response to Dr. Shoenfeld's expert report. Second Fife Rep. Dr. Fife discussed Dr. Shoenfeld's cited literature that indicated 10 cases of ILL were attributed to the influenza vaccine. Dr. Fife pointed out that each case cited by Dr. Shoenfeld was documented with bronchoscopy and lung biopsy and provided additional evidence of allergic-type reactions in the lungs. Second Fife Rep. at 1. No such tests were conducted in Mr. Feider's case. *Id*. Dr. Fife also indicated that although pneumonia "is the most common infectious cause of death in the U.S.", it is frequently culture negative, even with sepsis. *Id*. Dr. Fife defended his assertion by pointing out that pneumonia remained the consensus diagnosis of all providers who cared for Mr. Feider, and it was consistent with the clinical data. *Id.*

C. Respondent's Expert: Dr. Penelope Morel

1. Qualifications

Dr. Morel received her medical degree from the University of Southampton School of Medicine and received a doctor of medicine from the University of Geneva, Switzerland. Ex. D (hereinafter "Morel CV") at 1. Dr. Morel received training in rheumatology at Stanford University during a postdoctoral fellowship. Morel CV 1. Dr. Morel is currently a professor of immunology

and medicine at the University of Pittsburgh where she teaches medical, graduate, and undergraduate students immunology and directs a course for MD/PhD students on molecular medicine. *Id.* at 1-2. Although she does not presently see patients, she has been engaged in basic and clinical immunology research and has maintained an NIH funded laboratory since 1991. *Id.* at 1. Dr. Morel's primary area of research has been the field of autoimmunity. In particular, she has examined genetic predispositions in various human autoimmune conditions including T1D, rheumatoid arthritis, and systemic sclerosis focusing on human leukocyte antigen and Fc receptor alleles. *Id*. Dr. Morel has written over 70 peer-reviewed articles and 38 invited reviews or chapters. *Id.* at 2.

2. Expert Reports

Dr. Morel filed three expert reports in this case. Exs. C (hereinafter "First Morel Rep."), BB (hereinafter "Second Morel Rep."), and JJ (hereinafter "Third Morel Rep.").

In her first report, Dr. Morel opined that pneumonia induced Mr. Feider's inflammatory environment, and that his atherosclerosis, age, and possible production of alarmins from dead or dying cells contributed to an exaggerated pro-inflammatory cytokine response. First Morel Rep. at 3. Dr. Morel noted that, although Mr. Feider had signs suggestive of SIRS as Dr. Shoenfeld proposed, "including fever, high respiratory rate and elevated WBC count," SIRS has a very broad definition that is oversensitive. *Id*. Almost every patient admitted to the ICU fulfills the criteria for SIRS because non-infectious trauma, burns, and even relatively mild infections can result in SIRS symptoms. *Id*. Dr. Morel argued that, although Mr. Feider's cultures and serology tests came back negative, such results can occur in cases of severe sepsis with co-morbidities, and Mr. Feider had longstanding and severe atherosclerosis, chronic kidney disease, and hypertension. *Id.* Dr. Morel indicated that a study of 330 patients admitted to the hospital with acute myocardial infarction (MI) found that 209 of them had SIRS. *Id*. Dr. Morel pointed out that troponin levels in Mr. Feider were normal upon admission but rose substantially several hours later, and that this rise was indicative of ischemic myocardial injury. *Id.* at 2.

Dr. Morel also opined as to whether SIRS could be caused by vaccines, noting that there is no literature to suggest that any vaccine can lead to the set of symptoms defining SIRS. First Morel Rep. at 2. The pediatrics textbook Dr. Shoenfeld referenced to support his claim that vaccines can cause SIRS did not cite any literature to support that assertion, and Dr. Morel suggested that the textbook was probably outdated because it was published in 2011. *Id.* at 4. Dr. Morel noted that Mr. Feider's initial symptoms of warmth and fatigue passed after one day, and two studies examining the effects of combined flu and PCV13 vaccinations in over 1000 individuals in each respective study demonstrated slight increases in systemic side effects in subjects, but no serious adverse events as seen in diagnoses of SIRS. *Id.* at 2. A positive SIRS diagnosis requires a large surge in cytokine production that is detectable systemically, but most vaccines, including flu, do not increase cytokine levels sufficiently to be detected without ultra-sensitive assays, above 20 pg/ml. *Id.* at 5. Dr. Morel opined that Dr. Shoenfeld's studies alluded to cytokine release in response to vaccines that was detected following *in vitro* stimulation of cells rather than for systemic circulation. *Id*. One study that Dr. Shoenfeld referenced that did examine systemic circulation found the levels of some cytokines rise, but others fell, and all remained below detection levels without ultra-sensitive assays. *Id*.

Dr. Morel opined that reactions to influenza and pneumococcal vaccines that are administered in the arm are confined to the lymph node for T cells with specificity for influenza and pneumococcal antigens. First Morel Rep. at 5. Dr. Morel contrasted this with Dr. Shoenfeld's cited publication describing SIRS induction in six volunteers receiving mAb targeting CD28. *Id.* The antibody in that study was a superagonist that had high activity and caused "simultaneous activation of a very large number of T cells" when administered directly in the circulatory system. *Id*. Dr. Morel noted that this differs from the more limited activation observed with T cells with antigen specificity for influenza and pneumonia when vaccines are administered in the arm and that drain to the lymph node. *Id*. Dr. Morel also opined that Mr. Feider more likely had a secondary immune response because of pre-existing immunity from receiving the vaccines previously. A secondary immune response is characterized by a cytokine response peak at 12 hours that subsides within 24 hours post-vaccination. *Id.* at 4-5. In Mr. Feider's case, his deterioration that required hospitalization began three days later. *Id.*

Dr. Morel also addressed Dr. Shoenfeld's theory of vaccination-induced rhabdomyolysis and AKI. She opined that elevated urea and creatinine are indicative of AKI, while elevated levels of creatine kinase (CK) are indicative of rhabdomyolysis. First Morel Rep. at 3. Notably, Mr. Feider's urea and creatinine levels were elevated when he was admitted to the hospital, and there was other evidence supporting SIRS. *Id*. However, CK levels were normal at the time of hospital admittance and did not increase until ten days later. *Id*. According to Dr. Morel, this indicates rhabdomyolysis could not have occurred until later in Mr. Feider's case and was probably reflective of MODS. *Id*. Dr. Morel pointed out that the case reports Dr. Shoenfeld highlighted in which rhabdomyolysis occurred shortly after influenza vaccine had distinguishable facts from Mr. Feider's case. All patients in the case reports had muscle pain and weakness and high CK levels at the time of hospital admittance, while Mr. Feider symptoms did not include weakness or muscle pain, and initially included low CK levels. *Id.* at 6.

In her second report, Dr. Morel addressed the case reports cited by Dr. Shoenfeld describing severe reactions following influenza and/or pneumococcal vaccination. Although each cited case indicated a reaction of some kind, none of the cases noted disease following vaccination. Second Morel Rep. at 1. None of the cases were classified as SIRS, and no case cited led to MODS or death. *Id*. Dr. Morel discussed Dr. Shoenfeld's theory that Mr. Feider had an enhanced inflammatory environment and/or genetic predisposition that caused SIRS following vaccination that was characterized by high levels of circulating cytokines. *Id*. She stated that patients with cryopyrin-associated periodic syndrome (CAPS) in Dr. Shoenfeld's cited study developed local reactions within hours of receiving the vaccine, and all recovered in a few days, unlike Mr. Feider. *Id.* at 1-2. Cytokine levels in vaccination cases do not rise above ultrasensitive-assay detection levels, let alone the levels observed in diseases that cause cytokine storm responses, like SARS-CoV-2. *Id.* at 2. Dr. Morel also pointed out that CRP is a non-specific reactive protein that can be elevated in cases of infection, inflammation, and many other conditions, and may not be dispositive of SIRS. *Id*. Dr. Morel further opined that Mr. Feider's chronic kidney disease (CKD) was exacerbated by pneumonia and that this resulted in Mr. Feider developing AKI, not the vaccines he received. *Id.* at 2.

V. Applicable Law

A. Petitioner's Burden

Under the Vaccine Act, a petitioner may prevail in one of two ways. First, a petitioner may demonstrate that she suffered a "Table" injury—i.e., an injury listed on the Vaccine Injury Table that occurred within the time period provided in the Table. § 11(c)(1)(C)(i). "In such a case, causation is presumed." *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006); *see* § 13(a)(1)(B). Second, where the alleged injury is not listed in the Vaccine Injury Table, a petitioner may demonstrate that she suffered an "off-Table" injury. § 11(c)(1)(C)(ii).

For both Table and non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1324 (Fed. Cir. 2010); *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873* (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records of by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen*. *Althen* requires that petitioner establish by preponderant evidence that the vaccinations he received caused her injury "by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* at 1278.

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioner may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). Special Masters, despite their expertise, are not empowered by statute to conclusively resolve what are complex scientific and medical questions, and thus

scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Hum. Servs*., 121 Fed. Cl. 230, 245 (2015) ("[p]lausibility … in many cases may be enough to satisfy *Althen* prong one" (emphasis in original)), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017). But this does not negate or reduce a petitioner's ultimate burden to establish her overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs*., 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, because they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Hum. Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing … that mandates that the testimony of a treating physician is sacrosanct -- that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record -- including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs*., 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Health & Hum. Servs*., No. 06-522V 2011 WL 1935813 at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without op.*, 475 Fed. App'x 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs*., 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs*., 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand on other grounds*, 105

Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 952 (Fed. Cir. 2013). *Koehn v. Sec'y of Health & Hum. Servs*., No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Law Governing Analysis of Fact Evidence

The process for making factual determinations in Vaccine Program cases begins with analyzing the medical records, which are required to be filed with the petition. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs*., 3 F.3d 413, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records created contemporaneously with the events they describe are generally trustworthy because they "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions," where "accuracy has an extra premium." *Kirby v. Sec'y of Health & Hum. Servs.*, 997 F.3d 1378 (Fed. Cir. 2021) citing *Cucuras*, 993 F.2d at 1528. This presumption is based on the linked proposition that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11-685V, 2013 WL 1880825 at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013) *mot. for rev. denied*, 142 Fed. Cl. 247, 251-52 (2019), *vacated on other grounds and remanded*, 809 Fed. Appx. 843 (Fed. Cir. Apr. 7, 2020).

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475 at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony -- especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; see also *Murphy v. Sec'y of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, there are situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs.*, 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual

predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475 at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs.*, 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent and compelling." *Sanchez*, 2013 WL 1880825 at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs.*, No. 90-2808V, 1998 WL 408611 at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *LaLonde v. Sec'y of Health & Hum. Servs.*, 110 Fed. Cl. 184, 203-04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. Analysis of Expert Testimony

Establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of his or her claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (*citing Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora. *Daubert* factors are employed by judges to exclude evidence that is unreliable and potentially confusing to a jury. In Vaccine Program cases, these factors are used in the weighing of the reliability of scientific evidence. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate persuasiveness and reliability of expert testimony has routinely been upheld. *See*, e.g., *Snyder*, 88 Fed. Cl. at 743. In this matter, (as in numerous other Vaccine Program cases), *Daubert* has not

been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)). A "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Id.* at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. Consideration of Medical Literature

Finally, although this decision discusses some but not all of the medical literature in detail, I have reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Hum. Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

VI. Analysis

Under *Althen's* first prong, the causation theory must relate to the alleged injury. Petitioner must provide a "reputable" medical or scientific explanation, demonstrating that the vaccines received can cause the type of injury alleged. *Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355-56 (Fed. Cir. 2006). The theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). It must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

A. *Althen* Prong One

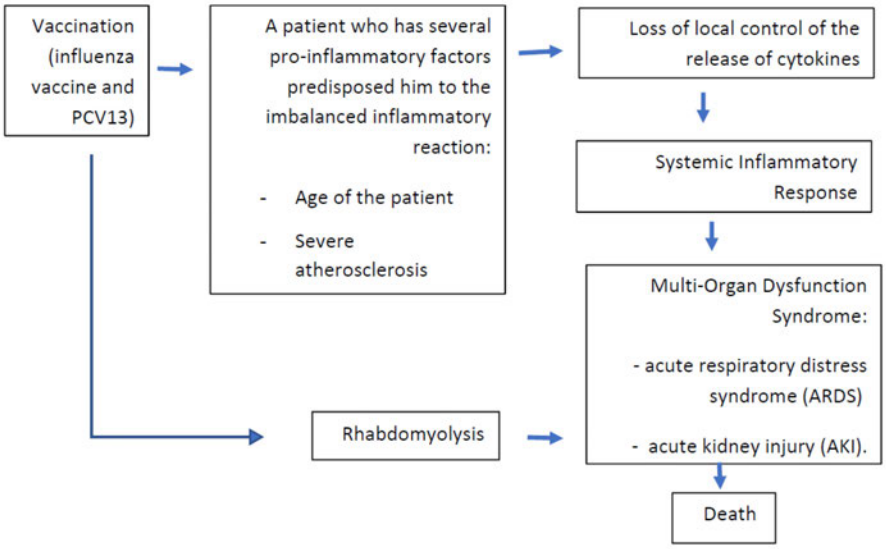
I note at the outset that Dr. Shoenfeld's causation theory is difficult to follow. It is unclear whether he opines that the flu and pneumococcal vaccines caused Mr. Feider to develop SIRS, which in turn led to ARDS and AKI, or whether Mr. Feider's vaccines caused him to develop

SIRS, ARDS, and AKI through separate processes. It also appears that Dr. Shoenfeld attributes rhabdomyolysis in Mr. Feider to a separate, vaccine-induced process.

> Petitioner ultimately summarized her theory of the case as follows:
>
> The increase of pro-inflammatory cytokines induced by vaccination contribute to the overall inflammatory context (taking into account the age of the patient and his severe atherosclerosis which are associated with the increased production of pro-inflammatory cytokines) and lead to the decompensation. Loss of local control of the release of the cytokines led to Systemic Inflammatory Response Syndrome (SIRS) and Multi-Organ Dysfunction Syndrome, which included acute respiratory distress syndrome (ARDS) and acute kidney injury (AKI). The Rhabdomyolysis, which occurred later in Mr. Feider['s] case, is also related to the influenza vaccine, since there are published case reports of rhabdomyolysis and AKI after influenza vaccine.

Shoenfeld Response to Questions at 1.[9]

> Dr. Shoenfeld provided the following flow chart to depict his causation theory in this case.



Shoenfeld Response to Questions at 1.

[9] However, in this same report, Dr. Shoenfeld similarly stated that Mr. Feider's ARDS was influenza vaccine-associated interstitial lung disease. *Id.* at 3. In a previous report, Dr. Shoenfeld supported his position that the vaccines Mr. Feider received caused him to develop ARDS. He said, "Case reports of Influenza vaccine-induced ILD [have] been published…" (Shoenfeld Response to Fife at 3), suggesting that the mechanism at play in this case is similar to those described in the case reports. Because it stretches reason to suggest that the flu and/or pneumococcal vaccines caused Mr. Feider to experience three separate vaccine reactions, I have analyzed Petitioner's prong one theory in terms of whether the flu/pneumococcal vaccines can cause SIRS, which subsequently leads to ARDS and AKI.

I note that in a different Vaccine Program case, a special master held that the petitioner established the MMR vaccine can cause SIRS, shock, and multiorgan dysfunction syndrome. *Ahlum v. Sec'y of Health & Hum. Servs.,* No. 12-763V, 2018 WL 4323623 (Fed. Cl. Spec. Mstr. Aug. 16, 2018). *See also, Bragg v. Sec'y of Health & Hum. Servs.,* No. 08-477V, 2012 WL 404773 (Fed. Cl. Spec. Mstr. Jan. 18, 2012) (finding that the flu vaccine can cause SIRS).

1. Flu Vaccine Can Cause SIRS

Following the vaccines on September 20, 2021, Mr. Feider reported feelings of warmth and fatigue on September 21 and 22. These symptoms abated on September 23, and Mr. Feider reported feeling back to normal until 11:00pm on September 24. Mr. Feider then reported feeling warm and having a shortness of breath. At the hospital, Mr. Feider had hypoxia, a fever, elevated respiratory and heart rates, and an elevated white blood cell count. Dr. Shoenfeld opined that these symptoms were consistent with the diagnostic criteria for SIRS, and Drs. Fife and Morel agreed.[10] First Shoenfeld Rep. at 11; Fife Rep at 2-3; First Morel Rep. at 3. *See also*, Respt's Post Hearing Brief at 13.

Dr. Shoenfeld opined with respect to the role of abnormal cytokine response in an immune-mediated inflammatory reaction to the influenza and pneumococcal vaccines. "It is well accepted that the loss of local control of the release of these cytokines leads to systemic inflammation and potentially deleterious consequences including the Systemic Inflammatory Response Syndrome . . . ." First Shoenfeld Rep. at 9.

In support of his position, Dr. Shoenfeld cited to Talaat et al., a study that reports the increase of specific cytokines within hours postvaccination. Talaat et al., *Rapid changes in serum cytokines and chemokines in response to inactivated influenza vaccination*, 12 INFLUENZA OTHER RESPI VIRUSES, 202-10 (2018) (filed as Ex. 18) (hereinafter "Talaat").

Dr. Shoenfeld also referenced Jaffer et al., *Cytokines in the systemic inflammatory response syndrome: a review*, 2 HSR PROC INTENSIVE CARE CARDIOVASC ANESTH 3, 161-75, 174 (2010) (filed as Ex. 35) (hereinafter "Jaffer"). Jaffer noted that "The inflammatory process involves the release of a pro- and anti- inflammatory cytokines. Anti-inflammatory cytokines act to localize and prevent over exuberant inflammation; it is a loss of this local control that leads to systemic inflammation and potential deleterious consequences, including SIRS . . . ." *Id.* at 162.

Such loss of local control over anti-inflammatory cytokines in immune response has been characterized in several different groups. One includes elderly subjects, who have been documented to have an impaired IFN-γ anti-inflammatory response. Bernstein et al., *Cytokine production after influenza vaccination in a healthy elderly population*, 16 VACCINE 18, 1722-31,

[10] As Dr. Morel noted in her report, "SIRS is defined by four variables: fever, tachycardia, increased respiratory rate and elevated white blood cell (WBC) count." First Morel Rep. at 3; *see also* Vincent et al., *Sepsis definitions: time for change*, 381 LANCET 774-75 (2013) (filed as Ex. J). Dr. Morel stated "[t]his a very broad definition and, as discussed in a recent article, it may be overly sensitive. Virtually every patient admitted to an ICU fulfils the criteria of SIRS since SIRS can be caused by many non-infectious processes including trauma, burns and ischemia reperfusion." First Morel Rep. at 3.

1723 (1998) (filed as Ex. 22). Another study noted "prolonged innate immune activation with impaired response in older adults . . . ." Mohanty et al., *Prolonged proinflammatory cytokine production in monocytes modulated by interleukin 10 after influenza vaccination in older adults*, 211 J INFECT DIS. 7, 1174-84, 1183 (2015) (filed as Ex. 23). Dr. Morel agreed that the elderly have an altered inflammatory response, "there is a progressive increase with age of the production of inflammatory cytokines," and opined that other chronic inflammatory conditions like atherosclerosis could produce a similar signature. First Morel Rep. at 3. Additionally, certain polymorphisms of cytokines and receptor antagonists of clinical relevance have been described as genetic predispositions for overactive systemic inflammatory reactions to influenza vaccines. Feezor, Moldawer, *Genetic Polymorphisms, Functional Genomics and the host Inflammatory Response to Injrut and Inflammation*, 9 FRONT IMMUNOL, 15-37 (2003) (filed as Ex. 25) (hereinafter "Feezor"). "[M]uch of the host response is a direct reflection of heritable trait, accounting for interpersonal differences, and allowing for genetic detection." Feezor at 15.

While inflammatory reactions to influenza vaccines and particular genetic predispositions are rare, as Drs. Fife and Morel point out, such occurrences have been documented, and they do occur. Von Elten et al., *Systemic inflammatory reaction after pneumococcal vaccine: A case series*, 10 HUM VACCINES IMMUNOTHER, 1767-70 (2014) (filed as Ex. 45) (hereinafter "Von Elten). "The 5 patients in this series all had leukocytosis, fever, and large local inflammatory reactions following influenza and PS23 vaccinations. Based on the known side effects of the PS23 vaccine . . . we believe these reactions were due to the PS23 vaccine." Von Elten at 1768. It is also notable that Mr. Feider had atherosclerosis, he was 71 when he died, and he fit within the age group described by Dr. Shoenfeld for a defective IFN-γ response that could lead to over compensatory production of pro-inflammatory TNFα. First Shoenfeld Rep. at 13; Bloch et al., *Production of TNF-alpha ex vivo is predictive of an immune response to flu vaccination in a frail elderly population*, 27 EUR CYTOKINE NETW. 3, 63-67 (2016) (filed as Ex. 24) (hereinafter "Bloch"). Bloch at 64.

I also note that Nelson Textbook of Pediatrics lists influenza vaccine reaction as a potential cause of SIRS. NELSON TEXTBOOK OF PEDIATRICS at 309 (Robert M. Kliegman et al. eds., 19th ed. 2011) (filed as Ex. 36) (hereinafter "Nelson Textbook of Pediatrics"). The fact that Nelson Textbook of Pediatrics is from 2011 and does not list references to support the assertion that vaccines can cause SIRS, as Dr. Morel stated (First Morel Rep. at 4), does not refute broad medical consensus. I find that Petitioner has presented preponderant evidence that the flu vaccine can cause SIRS.

2. Vaccine-Induced Rhabdomyolysis

Medical providers documented that Mr. Feider came into the hospital with identifiable AKI, and 10 days into treatment had severely elevated creatine kinase levels (37,258 U/l, normal range 21-232 U/l) that was indicative of rhabdomyolysis. Ex. 8 at 107; First Shoenfeld Rep. at 14.

Dr. Shoenfeld's theory shifted with respect to this issue. In his first report, filed on October 14, 2019, he opined as follows:

> In the case of [l]ate Mr. Feider, we confront concurrent systemic inflammatory response syndrome, respiratory failure with signs of interstitial lung disease and acute kidney injury probably resulting from rhabdomyolysis after concomitant administration of quadrivalent inactivated influenza vaccine and 13-valent pneumococcal conjugate vaccine, leading to his death.

First Shoenfeld Rep. at 9. In his report filed on April 20, 2020, Dr. Shoenfeld acknowledged that Mr. Feider's rhabdomyolysis did not cause his AKI. He stated:

> Dr. Morel states that since CK levels were normal at the time of admission, and they did not start to rise until 10 days into his course, on October 5, rabdomyolysis [sic] appears to have occurred late in Mr. Feider's case and was probably reflective of multiple organ dysfunction syndrome (MODS), but was not related to vaccination and did not cause acute kidney injury (AKI). While this appears to be true, we think that AKI in the case of Mr. Feider is still linked to vaccination. AKI is one of the most frequent organ dysfunctions in the course of SIRS. This is consistent with the fact, that Mr. Feider had SIRS, respiratory failure and AKI simultaneously at the time of hospital admission.

Shoenfeld Response to Morel at 4.

In his report responding to my questions, Dr. Shoenfeld opined that "The Rhabdomyolysis, which occurred later in Mr Feider['s] case, is also related to the influenza vaccine, since there are published case reports of rhabdomyolysis and AKI after influenza vaccine." Shoenfeld Response to Questions at 1.

As support for this most recent position, Dr. Shoenfeld cited cases of rhabdomyolysis-induced AKI following influenza vaccination. First Shoenfeld Rep. at 27-29, Table 1, entitled "Summary of cases of acute kidney injury following rhabdomyolysis after influenza vaccine." *See also* Patel & Shah, *Vaccine-Associated Kidney Diseases: A Narrative Review of the Literature*, 30 SAUDI J KIDNEY DIS TRANSPL 5, 1002-05 (2019) (filed as Ex. 59). These examples describe patients who complained of muscle pain and weakness following vaccination. Additionally, creatine kinase (CK) levels were well over the normal range, where five times the upper limit of normal is used as diagnostic criteria for rhabdomyolysis. First Shoenfeld Rep. at 14. Most cases developed symptomology within 1-2 days after vaccination, though several either had symptom onset or were admitted to the hospital as many as seven days after vaccination. *Id.* 27-29, Table 1. Other studies have established that an immune-mediated necrotizing myopathy (IMNM) and subsequent renal damage can occur related to statin/fibrate therapy or influenza infection, but the precise mechanism with infection is unclear. Allenbach et al., *224th ENMC International Workshop: Clinico-sero-pathological classification of immune-mediated necrotizing myopathies*, 28 NEUROMUSCUL DISORD 1, 87-99 (2016) (filed as Ex. 31) (hereinafter "Allenbach").

The evidence presented regarding whether the flu vaccine can cause rhabdomyolysis consists of case reports. While case reports are not robust evidence, they do constitute some evidence with which petitioners can meet their burden in the Vaccine Program. *See Contreras v. Sec'y of Health & Hum. Servs.*, 107 Fed. C. 280 (Fed. Cl. 2012); *see also Capizzano* 440 F.3d at

1325-26. However, in this case, it is undisputed that Mr. Feider developed rhabdomyolysis after AKI, and thus the rhabdomyolysis did not cause the AKI. *See* Ex. 8 at 916 (nephrologist on September 24, 2016 documenting "No rhabdomyolysis as [of] now. Will foll[o]w with CK level tomorrow."); First Morel Rep. at 6 (opining that Mr. Feider did not have rhabdomyolysis at the time of his hospital admission, and instead developed it 10 days later); Shoenfeld Response to Morel at 4 (agreeing with Dr. Morel that rhabdomyolysis occurred as a result of MODS). Because of this, I have not analyzed whether the flu vaccine can cause rhabdomyolysis.

3. MODS, ARDS, and AKI as Complications of SIRS

Dr. Shoenfeld noted that "[i]f the balance between pro- and anti- inflammatory cytokines is not maintained, dysregulation occurs leading to SIRS and multiple end organ effects", including ARDS, MODS, and AKI. First Shoenfeld Rep. at 10. "In people, MODS is most commonly a sequela to severe sepsis or septic shock, but it also develops secondary to trauma, neoplasia, or other causes of the systemic inflammatory response syndrome (SIRS)." Osterbur et al., *Multiple Organ Dysfunction Syndrome in Humans and Animals*, 28 J VET INTERN MED 4, 1141-51 (2014) (filed as Ex. 62) (hereinafter "Osterbur"). Osterbur at 1141. The uncontrolled inflammation seen in SIRS is also a central issue in the development of ALI and its more severe form, ARDS. Lin et al., *Regulatory T Cells and Acute Ling Injury: Cytokines, Uncontrolled Inflammation, and Therapeutic Implications*, 9 FRONT IMMUNOL 1545 (2018) (filed as Ex. 26) (hereinafter "Lin"). *See also* Nelson's Textbook of Pediatrics at 4 (stating that "[t]he inflammatory cascade initiated by shock can lead to … acute respiratory distress syndrome (ARDS)."

Notably, "[s]everal studies have also reported a number of cytokines – such as TNF- α, IL-1B, IL-6, IL-17, and IL-33 – were increased in the acute stages of ARDS/ALI", the same cytokines overproduced in patients with abnormal cytokine responses. Lin at 1; Bloch at 64. Relatedly, both ARDS and AKI have been found to be frequent complications of SIRS. Chakraborty & Burns, *Systemic Inflammatory Response Syndrome*, STATPEARLS PUBLISHING (2020) (filed as Ex. 58) (hereinafter "Chakraborty"). Chakraborty at 10. Abnormal TNF-α and endotoxin production appear to be predominant mechanisms for inducing apoptosis and AKI in certain forms of MODS, and Dr. Morel conceded that AKI is common in patients with severe sepsis. Osterbur at 1145; Ex. JJ at 1. Therefore, Dr. Shoenfeld's assertions that SIRS can cause the MODS, ARDS, and AKI are supported by preponderant evidence.

B. *Althen* Prong Two

Under *Althen's* second prong, a petitioner must "prove a logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Althen*, 418 F.3d at 1278. The sequence of cause and effect must be "'logical' and legally probable, not medically or scientifically certain." *Id.* A petitioner is not required to show "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." *Id.* (omitting internal citations). *Capizzano*, 440 F.3d at 1325. Instead, circumstantial evidence and reliable medical opinions may be sufficient to satisfy the second *Althen* prong.

1. Preponderant Evidence Demonstrates that Mr. Feider was Unwell the Day of and the Day after Vaccination Followed by an Improvement in his Symptoms before his Hospitalization, a Clinical Course that is Inconsistent with Petitioner's Prong One Theory

The medical records document that Mr. Feider received the flu and pneumonia vaccines on Tuesday, September 20, 2016; then the records demonstrate that he felt unwell on Wednesday, September 21; he was improved on Thursday, September 22 and Friday September 23 such that he went about his normal activities. Then on September 23 at around 11:00pm, Mr. Feider experienced a sudden onset of shortness of breath and difficulty breathing.

The Buffalo VA Hospital ER department's medical records from September 24, 2016 document that Mr. Feider reported receiving the influenza and pneumococcal vaccines on September 20th and the following day, developed a cough, felt feverish and unwell. Ex. 8 at 982. By Thursday, September 22, 2016, Mr. Feider indicated that he felt "much improved." *Id.* He also felt well on Friday, September 23rd until 11:00pm that night when he experienced a sudden onset of shortness of breath and difficulty breathing. *Id.*

During an examination on September 24, 2016, Dr. Jaime Bittner recorded the following history of present illness:

> Patient presents with a one day history of sudden SOB (shortness of breath) with fever. Patient felt relatively healthy yesterday and went to his usual cardio rehab, went home had lunch, went out to dinner and felt like his usual self. He was watching TV last night and at 11pm began to feel warm, shaky, and had a "tough time breathing"…. Patient got a Flu shot and pneumovax on Tuesday, then felt warm and slept all day Wednesday but was back to his usual state of health by Thursday.

Ex. 8 at 946.

Additionally, the medical records from a different consultation on September 24, 2016 document that Mr. Feider received the flu and pneumonia vaccines on September 20, and that evening began having "some myalgias and subjective fever." Ex. 8 at 353. The record notes that Mr. Feider did not check his temperature. *Id.* These symptoms persisted all day on Wednesday. *Id.* This medical record notes that Mr. Feider "recovered well [] on Thursday." *Id.* The record then states that Mr. Feider "felt increasing dyspnoeic [sic] overnight with cough and productive of sputum with fever from evening. y'day." *Id.*

Petitioner's affidavit described a history on the day of vaccination and the next day (Tuesday, September 20 and Wednesday, September 21) that is consistent with the medical records. Ms. Switzer averred that within a couple of hours post-vaccination, Mr. Feider began to feel unwell. Ex. 1 at 2. According to Petitioner, Mr. Feider "had a headache [] was feeling tired and achy and went to bed early." *Id.* Petitioner stated that on Wednesday, Mr. Feider spent most of the day in bed or on the couch "with a fever and flu like symptoms." *Id.* These assertions are supported by the medical records discussed above.

However, in describing Mr. Feider's condition on Thursday, September 22 and Friday, September 23, Ms. Switzer provided a different account than the contemporaneous medical records. She stated, "[h]e continued to have these symptoms [a fever and flu-like symptoms] on Thursday and Friday as well. Both nights he awoke with night sweats so badly that the sheets needed to be changed." Ex. 1 at 2. This account differs from Mr. Feider's statements upon his ER admission and to Dr. Bittner where he indicated that by Thursday he was "much improved" and "back to his usual state of health", and that on Friday, he "felt well" and "felt like his usual self." Ex. 8 at 982; Ex. 4 at 946.

Contemporaneous medical records generally deserve greater evidentiary weight than oral testimony -- especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; see also *Murphy v. Sec'y of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

Petitioner contends that her affidavit is not inconsistent with the medical records, and points to two records which do not discuss Mr. Feider's improvement. Pet'r's Reply 1-2 (citing Ex. 8 at 343-45; Ex. 8 at 300). The first record is from a cardiology consultation which took place on September 24, 2016. Ex. 8 at 343. This record documents the following:

> According to the patient, he received influenza and pneumococcal immunization on Tuesday September 20th. He then states the following day (Wednesday), he started having cough and feeling warm and unwell. Late Friday evening he started developing difficulty breathing, along with cough and some sputum and so called ambulance [due to] worsening breathing…

Ex. 8 at 343. This record does not discuss how Mr. Feider was feeling on Thursday or on Friday before the late evening. Accordingly, while this record is not inconsistent with Petitioner's affidavit, it does not support the contested point that Mr. Feider remained in poor health during this period of time.

Petitioner also pointed to a pulmonary consultation on October 3, 2016 with Dr. Sarkis as support for her claim in her affidavit that Mr. Feider was still sick on Thursday and Friday. The notes from this visit indicate that Mr. Feider

> presented on 9/24 for hypoxemia, respiratory distress. He was at his baseline prior to admission (runs 0.5 mile on treadmill, attends cardiac rehab), up until he received flu and pneumonia vaccine on 9/20. Since, he started complaining of worsening dyspnea, productive cough.

Ex. 8 at 300. This record is similarly silent regarding Mr. Feider's state of health on Thursday September 22 and Friday September 23rd. Like the cardiology consultation from September 24, 2016, this record does not speak to how Mr. Feider was feeling during this timeframe. Because of

that, I have credited the detailed contemporaneous medical records over these less detailed records and Petitioner's affidavit. It is difficult to imagine that Mr. Feider erroneously provided the same history of a recovery on Thursday and most of the day on Friday to three different medical providers.

Petitioner suggests that the contemporaneous medical records lack information about Mr. Feider's poor health on Thursday and Friday because he was unwell with a fever of 104.5˚ upon presentation and likely had "difficulty relaying a complete history." Pet'r's Reply at 2. This argument is unavailing as Mr. Feider's initial ER admission, when he was extremely unwell, makes note of his improved condition on Thursday and Friday. *See* Ex. 8 at 982.

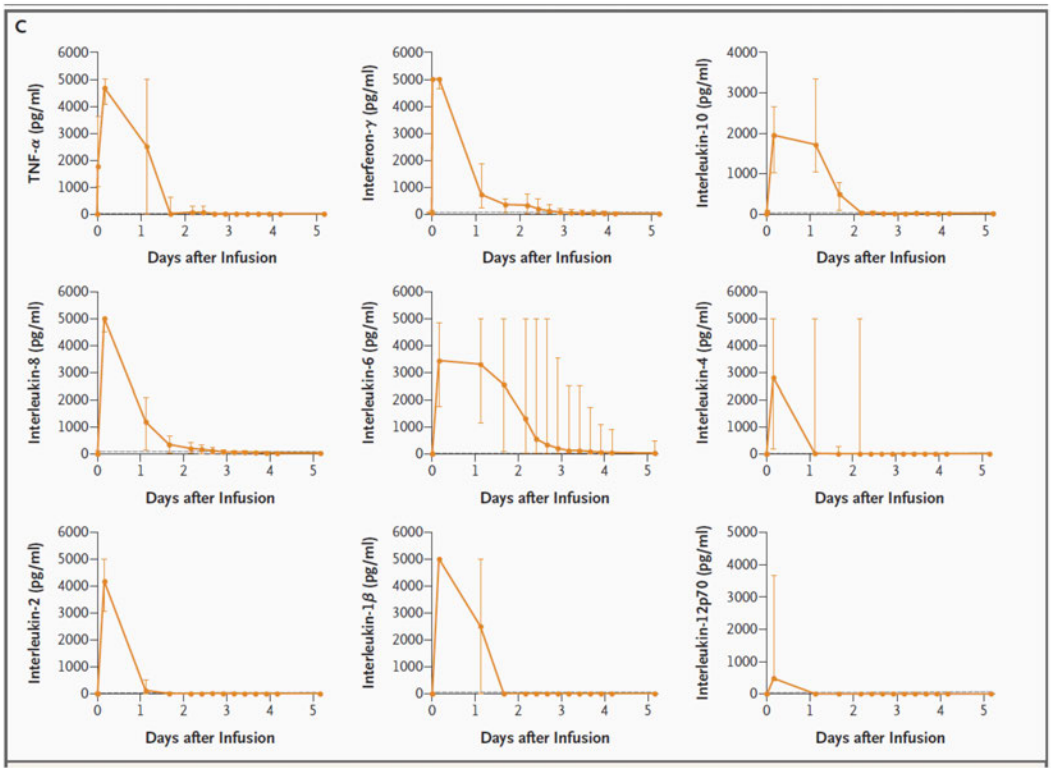
Petitioner additionally attempts to explain this one and one half day recovery by noting that Mr. Feider was taking Motrin and drinking fluids. Pet'r's Reply at 3. Petitioner points to a medical record from September 24, 2016 in support of her position. This record documents: "He took motrin, OTC tab 2 days ago for myalgias." Ex. 8 at 916. While two days before September 24 is September 22, I find this record only provides minimal support for Petitioner's position. As discussed extensively above, no medical record documents that Mr. Feider was experiencing myalgias on September 22. In fact, the records that discuss how he was feeling on this date all document that he was much improved and back to his normal state of health. I therefore find it is likely that the myalgias referenced in this note include Mr. Feider's reported myalgias from September 21, that are documented in this same medical record. See *id.* at 911. This note indicating Mr. Feider took Motrin two days ago does not overcome the weight of the medical record evidence in this case. Further, Petitioner's argument that Mr. Feider was taking Motrin and drinking fluids (and thus felt better) does not account for the fact that Mr. Feider described that he was "back to his usual state of health" by Thursday. Being back to one's normal state of health is different than feeling improvement due to self-medication.

Ultimately, this point is an important one, as Mr. Feider's one and one half day recovery is inconsistent with Petitioner's theory of causation, which relies on the overproduction of cytokines. Talaat et al. studied cytokine response in 20 healthy adults after they received the influenza vaccine. Talaat noted the following: "In our study, we extend our analysis into the first hours following TIV administration and identified temporal patterns of serum cytokine and chemokine changes which occurred as early as 3 hours postimmunization, generally peaking at approximately 24 hours." Talaat at 207. Talaat demonstrates that cytokines peak within 24 hours after vaccination.

Petitioner's contention that intravenous drug dosing of monoclonal antibody (mAb) mirrored the progression of Mr. Feider's course is also inconsistent with Petitioner's causation theory. The study notes the following:

> Within 90 minutes after receiving a single intravenous dose of the drug, all six volunteers had a systemic inflammatory response characterized by a rapid induction of proinflammatory cytokines and accompanied by headache, myalgias, nausea, diarrhea, erythema, vasodilatation, and hypotension. Within 12 to 16 hours after infusion, they became critically ill, with pulmonary infiltrates and lung injury, renal failure, and disseminated intravascular coagulation.

Suntharalingam et al., *Cytokine Storm in a Phase 1 Trial of the Anti-CD28 Monoclonal Antibody TGN1412*, 355 N ENGL J MED 10, 1018-28 (2006) (filed as Ex. 39) (hereinafter "Suntharalingam"). Suntharalingam at 1018. The following charts depict the rapid increase and then decrease in cytokines after infusion of TGN1412.



Id. at 1025. Similar to Talaat, this study depicts the rapidity of the cytokine response.

Respondent provided a study that also demonstrated a short temporal pattern for cytokine changes postimmunization in the lymph node, where the majority of cytokines are confined and produced. Chatziandreou et al., *Macrophage Death following Influenza Vaccination Initiates the Inflammatory Response that Promotes Dendritic Cell Function in the Draining Lymph Node*, 18 CELL REP 10, 2427-40 (2017) (filed as Ex. 27-20) (hereinafter "Chatziandreou").

The Chatziandreou study states the following:

> Among the tested cytokines, we detected a rapid and significant secretion of IL-1α and IFN-β in the LN within the first 90 min p.v. To evaluate the duration and magnitude of the inflammatory reaction, we examined the levels of additional inflammatory molecules in the first 24 hr p.v. We observed a significant peak in the secretion of MIG, IP-10, KC, MCP-1, MIP-1α, and MIP-1β at 12 hr, followed by an abrupt decrease by 24 hr p.v."

Id. at 2431.

Petitioner's study shows that severe local reactions occur within hours of receiving the vaccine and continue without an intermission of symptoms for persons with genetic predispositions for immune response, such as cryopyrin-associated periodic syndrome (CAPS). Walker et al., *Brief Report: Severe Inflammation Following Vaccination Against Streptococcus pneumoniae in Patients with Cryopyrin-Associated Periodic Syndromes*, 68 ARTHRITIS & RHEUMATOLOGY 2, 516-20 (2017) (filed as Ex. 51). "The local adverse reaction to the PPV23 was similar in all patients and developed a few hours after the injection, with pain, redness, and local swelling." *Id.* at 518.

The medical literature suggests that vaccination would have induced an immediate surge in cytokine production if Mr. Feider had an inflammatory immune response, and is inconsistent with Petitioner's claim that "[t]his mirrors the progression of Mr. Feider's course."[11] First Shoenfeld Rep. at 12. The medical records are clear and indicate that Mr. Feider's course included one and one half days of improvement between the time of vaccination on September 20, 2016 and hospital evaluation on September 24, 2016. Ex. 8 at 982. As Dr. Morel pointed out, any immune response to the vaccines "would have subsided by 24 hrs post-vaccination and could not have led to the development of SIRS, that began 3 days after Mr. Feider received his vaccines." First Morel Rep. at 4.

I gave Dr. Shoenfeld an opportunity to address the question of Mr. Feider's improvement. In an order directing the experts to answer several of my questions, I posed the following question to Dr. Shoenfeld: "How does the fact that Petitioner was feeling better fit into the theory that Petitioner's injury was caused by a cytokine cascade?" *See* Order dated Aug. 21, 2020; ECF No. 35. Dr. Shoenfeld responded as follows: "Actually, the Petitioner states that Mr. Feider continue[d] to have fever and flu-like symptoms on Wednesday, Thursday and Friday before he was transported by the ambulance to the hospital. So Mr. Feider did not feel better." Shoenfeld Response to Questions at 2. This statement failed to answer my question, and is belied by the medical records, discussed herein. *See Burns v. Sec'y of Health & Hum. Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993) (stating that a special master need not credit the opinion of an expert when the expert "based his opinion on facts not substantiated by the record."). In sum, the one and one half day improvement in Mr. Feider's clinical course is inconsistent with his theory of causation and

[11] Petitioner's claims about vaccine-induced rhabdomyolysis are similarly suspect. The studies cited by Petitioner indicate that creatine kinase (CK) levels, an important marker used in diagnosing and assessing rhabdomyolysis, "rise approximately 2 to 12 hours after the onset of muscle injury, peak[] within 24 to 72 hours, and then decline[] at the relatively constant rate of 39% of the previous day's value", where maintenance of CK levels may be indicative of a syndrome. Khan, Hospital, *Rhabdomyolysis*, 67 NETH J MED 9, 272-83 (2009) (filed as Ex. 28) (hereinafter "Khan"). Khan at 276. As Dr. Shoenfeld conceded, Mr. Feider's CK levels were normal at the time of hospital admission, and "r[h]abdomyolysis appears to have occurred late in Mr. Feider's case" when CK levels rose 10 days into treatment, itself more than three days after vaccination. Shoenfeld Response to Morel at 4. Notably, seven out of nine of Petitioner's own cases indicate rhabdomyolysis following influenza vaccination had symptom onset within 48 hours of vaccination, and the remaining were noted within seven days without a clear indication of time of symptom onset. First Shoenfeld Rep. at 27-29, Table 1. Additionally, the studies cited by Dr. Shoenfeld refer to statin therapy and influenza causes of rhabdomyolysis. *Id.* at 15. The connection between these studies and influenza vaccination is unpersuasive and unresolved by Dr. Shoenfeld's discussion of statin-induced muscle toxicity. *Id.*

means that Petitioner cannot meet her burden of establishing that the vaccine "did cause" Mr. Feider's condition.

2. Mr. Feider's Diagnosis of Community-Acquired Pneumonia is Supported by the Record

Community-acquired pneumonia is very common, accounting for as many as 500,000 hospitalized cases per year; pneumonia is recognized as the most common infectious cause of death in the United States. Second Fife Rep. at 1; Marston et al., *Incidence of community-acquired pneumonia requiring hospitalization. Results of a population-based active surveillance Study in Ohio*, 157 ARCH INTERN MED 15, 1709-18 (1997) (filed as Ex. CC); Miniño et al., *Deaths: final data for 2008*, 59 NATL VITAL STATE REP, 1-126 (2011) (filed as Ex. EE). Despite its frequency, many patients who are diagnosed with community-acquired pneumonia culture negative, even with sepsis. Mosevell et al., *Inflammatory Mediator Profiles Differ in Sepsis Patients With and Without Bacteremia*, 9 FRONT IMMUNOL, 691 (2018) (filed as Ex. DD).

Mr. Feider's treating physicians consistently documented that he likely suffered from community-acquired pneumonia. *See, e.g.*, Ex. 8 at 358 (noting clinical picture of pneumonia); Ex. 8 at 381 (assessing "respiratory failure secondary to pneumonia vs. CHF exacerbation"); Ex. 8 at 384 (documenting "AKI aft[e]r viral pneumonia"); Ex. 8 at 394 (stating "PVD admitted for Parainfl[ue]nza viral pneumonia with a complicated course since then with multiorgan failure"); Ex. 8 at 405 (noting a primary diagnosis of "resp failure. probable pneumonia"); Ex. 8 at 990 (documenting that "Pt has febrile picture w/ cough 3 days ago that was th[]ought to be resolving but blossomed tonight w/ SOB and hypoxia which certainly can be caused by his CHF and pneumonia."). Ex. 8 at 916 (noting "72 yo male with h/o recent flu shot 43 [sic] days ago, followed by worseni[ng] cough and dyspoea [sic] with fever, myalgias, with clinical picture with Pneumonia, espe Rt side -lower and mid zones…"). None of his treating physicians attributed Mr. Feider's clinical course to the vaccines he received. His primary diagnosis after his death was multiple organ dysfunction syndrome. Ex. 8 at 248. Community-acquired pneumonia was listed as a secondary diagnosis. *Id.*

In weighing evidence, special masters are expected to consider the views of treating doctors. *Capizzano*, 440 F.3d at 1326. The views of treating doctors about the appropriate diagnosis are often persuasive because the doctors have direct experience with the patient whom they are diagnosing. *See McCulloch v. Sec'y of Health & Hum. Servs.*, No. 09-293V, 2015 WL 3640610, at *20 (Fed. Cl. Spec. Mstr. May 22, 2015).

In addition to some of his treating physicians, both Dr. Morel and Dr. Fife opined that Mr. Feider suffered from community-acquired pneumonia. First Fife Rep. at 3; Second Fife Rep. at 1; Third Fife Rep. at 1; First Morel Rep. at 6; Second Morel Rep. at 2; Third Morel Rep. at 2.[12]

[12] Of note, Dr. Morel also opined that AKI is "quite common" in cases of community-acquired pneumonia. Third Morel Rep. at 1. She went on to state that "Mr. Feider had long[]standing CKD with severely reduced blood supply to one of his kidneys and compromised circulation to the other one. Thus, he was most vulnerable to additional AKI when he acquired pneumonia." *Id.* at 1-2.

Dr Shoenfeld opined that Mr. Feider did not suffer from community-acquired pneumonia because he had negative blood and sputum tests, and because he did not respond to antibiotics.

Dr. Fife opined that although Mr. Feider's sputum smear and bronchoalveolar lavage lacked evidence of infection, this result should have been unsurprising because Mr. Feider was treated with antibiotics for 10 days before the samples were taken. Third Fife Rep at 1. Additionally, such tests come back positive in only around one-third of cases of community-acquired pneumonia. First Fife Rep. at 3. Rosón et al., *Prospective Study of the Usefulness of Sputum Gram Stain in the Initial Approach to Community-Acquired Pneumonia Requiring Hospitalization*, 31 CLIN INFECT DIS, 869-74 (2000); (filed as Ex. G). Additionally, Dr. Fife noted that "nearly half of all cases of severe sepsis have negative blood cultures." First Fife Rep. at 3. *See also* Gupta et al., *Culture-Negative Severe Sepsis Nationwide Trends and Outcomes*, 150 CHEST,1251-59 (2016) (filed as Ex. H). Dr. Morel agreed with Dr. Fife, stating that "all cultures and serology tests came back negative, which is not unusual in cases of severe sepsis with co-morbidities." First Morel Rep. at 3.

Petitioner alleges Mr. Feider's failure to respond to antibiotics suggests that the "relationship between the vaccines, received by the patient, and his health problems appear[s] to be more credible" than the diagnosis of community-acquired pneumonia. Shoenfeld Response to Fife. at 3. Dr. Shoenfeld emphasized this point, quoting the Infectious Disease Society of America guidelines which state that "treatment failure, deterioration or progression in hospitalized patients with community-acquired pneumonia should [only] be considered after 72 h of initial treatment with antibiotics."[13] *Id.* at 2.

Certainly if Mr. Feider had responded to antibiotics, the question of whether he had a bacterial infection would be moot. However, the fact that he did not respond to antibiotics does not provide conclusive evidence that Mr. Feider did not have community-acquired pneumonia.

Ultimately, the question of diagnosis is a difficult one that Mr. Feider's treating physicians struggled with. The medical evidence presented on this point suggests that Mr. Feider likely had community-acquired pneumonia, a fact which further reduces the strength of Petitioner's showing under the second *Althen* prong. *Stone/Hammit v. Sec'y of Health & Hum. Servs.*, 676 F.3d 1373, 1380 (Fed. Cir. 2012).

I conclude that the course of Mr. Feider's illness, which included a one and one half day improvement in symptoms, is not consistent with Dr. Shoenfeld's cytokine-based theory of causation. Further, the fact that Mr. Feider's treating physicians reasonably considered community-acquired pneumonia as his correct diagnosis causes me to conclude that Petitioner has failed to establish the vaccines Mr. Feider received "did cause" his condition.

[13] I note that Dr. Shoenfeld omitted the word "only" between the words "should" and "be". First Shoenfeld Rep. at 3; Goncalves at 6.

C. *Althen* Prong Three

The timing prong contains two parts. First, a petitioner must establish the "timeframe for which it is medically acceptable to infer causation" and second, she must demonstrate that the onset of the disease occurred in this period. *Shapiro v. Sec'y of Health & Hum. Servs.,* 101 Fed. Cl. 532, 542-43 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 952 (Fed. Cir. 2013).

Dr. Shoenfeld spent little time discussing how Petitioner satisfied the third *Althen* prong. He opined that "[t]he time of the symptoms' onset coincided with the period of cytokine response to the influenza vaccination." First Shoenfeld Rep. at 13.

Petitioner reinforced this point in her brief and in her reply brief. She stated: "Mr. Feider's onset of systemic symptoms "within a couple of hours" fits perfectly within the expected timeframe of an initial cytokine response to vaccination." [14] Pet'r's Reply at 18; *see also* Pet'r's Post-Hearing Brief at 34. Petitioner continued, stating that "[a]fter producing a cytokine response to vaccination, Mr. Feider then continued to progress to a dysregulated SIRS reaction, meaning the anti-inflammatory cytokines failed to arrest the cytokine storm." Pet'r's Reply at 12.

As discussed earlier in this decision, I find that Mr. Feider experienced myalgias, subjective fever, and felt generally unwell the day of and the day after vaccination. He was then "much improved" within 48 hours of vaccination and returned to his "usual state of health". Ex. 8 at 946, 982. He remained well for one and one half days and then developed a sudden onset of shortness of breath and difficulty breathing. *Id.* at 982.

Dr. Morel opined that any immune response to the vaccines "would have subsided by 24 hrs post-vaccination and could not have led to the development of SIRS, that began 3 days after Mr. Feider received his vaccines." Morel Rep. at 4. This opinion is consistent with the medical literature filed in this case. *See e.g.,* Chatziandreou, Talaat.

Accordingly, I find that the onset of Mr. Feider's illness that eventually led to his death did not occur "within a couple of hours" of vaccination. Instead, Mr. Feider suffered general side effects from his vaccines, from which he recovered; he then developed a sudden onset of shortness of breath and difficulty breathing three and one half days after vaccination. Petitioner has not presented preponderant evidence that this onset interval is medically acceptable to infer vaccine causation, given his cytokine-based theory. Because of this, Petitioner has not presented preponderant evidence with respect to the third *Althen* prong.

VII. CONCLUSION

This is a tragic case and I extend my sympathy to Ms. Switzer's family for their loss.

[14] Petitioner cited to the Talaat study, noting that it "addresses the timing of the cytokine response after the influenza vaccination." Pet'r's Post-Hearing Brief at 34. Indeed, Talaat concluded that "[s]erum cytokines changed rapidly following TIV and generally peaked at 24 hours." Talaat at 202.

However, upon careful evaluation of all the evidence submitted in this matter, including the medical records, medical literature, the affidavits, as well as the experts' opinions, I conclude that Petitioner has not shown by preponderant evidence that she is entitled to compensation under the Vaccine Act. **Her petition is therefore DISMISSED. The clerk shall enter judgment accordingly.**[15]

IT IS SO ORDERED.

s/ Katherine E. Oler
Katherine E. Oler
Special Master

[15] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by each filing (either jointly or separately) a notice renouncing their right to seek review.